REMARKS

The non-elected claims belonging to restriction Groups II, III and V to VII have been amended to place them in a form more consistent with U.S. patent practice. The amendments do not narrow the scope of the claims. When the claims of Group I have been allowed, applicants will request that the claims of at least one of these other groups (methods using the composition of Group I) be rejoined. Therefore, it is requested that these amendments be entered, even though the claims have been (prematurely) withdrawn from consideration.

New claim 30 recites an aspect which was recited in original claim 7; it belongs in the restriction group to which claim 7 has been assigned, group III. New claims 31-34 recite specific aspects recited in original claim 9; they belong in the restriction group(s) to which claim 9 has been assigned. New claim 35 belongs in restriction group I, claims 36 and 37 in restriction group II.

With regard to the rejection under 35 USC 112, second paragraph, concerning the sequence of CD55, the primary sequence is well-known and readily available to the public. For example, the specification clearly teaches (*e.g.*, at page 29, lines 6-7) that the primary sequence of CD 55 can be found in GenBank, accession no. M31516. Also, see Fig. 1b, which presents the sequence of the protein by nanoelectrospray-tandem-mass spectroscopy.

With regard to the alleged "requirement" to deposit a hybridoma cell line that produces monoclonal antibody SC-1, such a deposit is not required to satisfy the requirements of 35 USC 112, first paragraph. The instant specification clearly teaches that a hybridoma cell line for generating such an antibody can be routinely generated, using, *e.g.*, the procedure disclosed in Vollmers *et al.* (1989), *Cancer Research* 49, 2471-2476 (see, *e.g.*, the specification at page 19, lines 11-13), which is incorporated in its entirety therein. That is, the instant specification teaches one of ordinary skill in the art to generate an antibody which at least has substantially the same properties as the SC-1 antibody.

Case law dictates that this is so.

In *Hybritech Inc. v. Abbott Laboratories*, 4 USPQ2d 1001 (U.S. Court Central District of California, 1987), the court ruled, with respect to whether a deposit of a monoclonal antibody is required in order to meet the enablement requirement:

It is well settled, however, that biological materials need not be deposited when the invention can be practiced without undue experimentation from biological materials available in prior art. *In re Argoudelis*, 168 USPQ 99 (CCPA 1970). In *MAB*, the Federal Circuit held that the record fully supported Hybritech's statement that "[t]he monoclonal antibodies used for the present invention are obtained by the [hybridoma] process discussed by Milstein and Kohler" and that the "details of this process are well known."(citing *Hybritech v. Monoclonal Antibodies*, 231 USPQ 81 (Fed. Cir. 1986), at 93) ... Thus, the Federal Circuit seems to have determined that this is not a case that would raise the question of whether biological materials need to be deposited according to *Lundak*.

In *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), the Federal Circuit ruled, with respect to whether a deposit of a monoclonal antibody is required in order to meet the enablement requirement:

Although inventions involving microorganisms or other living cells often can be enabled by a deposit, a deposit is not always necessary to satisfy the enablement requirement. No deposit is necessary if the biological organisms can be obtained through routine screening that does not require undue experimentation. ... Wands states that application of [methods which are well known in the monoclonal antibody art] requires only routine screening, and that does not amount to undue experimentation. There is no challenge to their contention that the starting materials ... are available to the public. The PTO concedes that the methods used to prepare hybridomas and to screen them for high-affinity IgM antibodies against HBSAg were either well known in the monoclonal antibody art or adequately described in [the patent]. This is consistent with this court's recognition with respect to another patent application that methods for obtaining and screening monoclonal antibodies were well known in 1980 [again citing *Hybritech*, 231 USPQ at 94).

Most pertinent is *Amgen v. Chugai*, 18 USPQ2d 1016 (Fed. Cir. 1991). This concerned best mode and the deposit, as here, of a specific cell line, *i.e.*, a CHO cell line transfected by a plasmid encoding human EPO. The Federal Circuit ruled:

When a biological sample required for the practice of an invention is obtained form nature, the invention may be incapable of being practiced without access to that organism. Hence the deposit is required in that case. On the other hand, when, as is the case here, the organism is created by insertion of genetic material into a cell obtained from generally available sources, then all that is required is a description of the best mode and an adequate description of the means of carrying out the invention, not deposit of the cells. If the cells can be prepared without undue experimentation, a deposit is not required. ... Since the court found that that is the case here, we therefore hold that there is no failure to comply with the best mode requirement for lack of a deposit of the CHO cells, when the best mode of preparing the cells has been disclosed and the best mode cells have been enabled.

Defendants also assert that the record shows that scientists were unable to duplicate Lin's genetically-heterogenous best mode cell strain. However, we have long held that the issue is whether the disclosure is "adequate," **not that an exact duplication is necessary**. Indeed, the district court stated that the testimony is clear that no scientist could ever duplicate exactly the best mode used by Amgen, but that those of ordinary could produce mammalian host cell strain or lines **with similar levels of production** identified in Example 10. 13 U.S.P.Q.2d at 1774. What is required is an adequate disclosure of the best mode, not a guarantee that every aspect of the specification be **precisely and universally reproducible**. *See In re Gay,* 309 F.2d 769, 773, 135 U.S.P.Q. 311, 316 (CCPA 1962).

As for a deposit of the cell line, 23132, this cell line has been deposited in the German Collection of Microorganisms and Cell Culture Gmbh, Braunschweig (Brunswick) under file number DSM ACC 201, under conditions which meet the criteria set forth in MPEP 6-8.01 (p) (C), items 1-3. A Declaration under 37 CFR 1.132 to this effect will be submitted shortly.

Contrary to the allegation of the Examiner, neither Medof nor Tsuji anticipates the instant claims. The instant claims recite, *e.g.*, that the claimed glycoprotein comprises a "tumor-specific glycostructure," whereas the glycoproteins of Medof and Tsuji are both isolated from non-tumor tissue and do not comprise the recited tumor-specific glycostructure. The difference between the glycoproteins of the instant claims and the references is evidenced, *e.g.*, by their different molecular weights. The instantly claimed glycoprotein, which is isolated from tumor cells, such as human adenocarcinoma cell lines 23132, 3051 or 2957, or primary tumor cells of gastric adenocarcinoma patients, has a molecular weight of about 82 kD. See, *e.g.*, the instant specification at page 5, lines 12-18. By contrast, the glycoproteins of the references are isolated from non-tumor cells (human blood cells) and exhibit molecular weights which are not 82 kD, the difference in molelcular weight reflecting the molecular weight of the glycostructures. In Medof, the glycoprotein is isolated from human red cells (see, *e.g.*, the sentence beginning at the last line of page 1558) and has a molecular weight on SDS-PAGE of 70,000 (see, *e.g.*, page 1560, last 6 lines of the section entitled "Purification and Characterization of DAF"; page 1562, second full paragraph; and Fig. 2). In Tsuji, as the Examiner admits, DAF is purified from (non-tumor) human blood. Although the molecular weight of Tsuji's DAF is not disclosed in the reference, the Examiner has presented no reasons or evidence that this DAF, from non-tumor cells, has the claimed "tumor-specific" glycostucture. The glycoproteins of the references lack

all of the material elements of the claimed glycoprotein (*e.g.*, they are not tumor-specific), and thus do not anticipate the claimed glycoproteins. *In re Marshall*, 198 USPQ 344 (CCPA 1978).

Furthermore, in the glycoprotein recited in claim 2, the glycostructure reacts with monoclonal antibody SC-1. The references of record do not suggest or disclose that the glycoproteins described therein react with SC-1. This is yet another feature which distinguishes claim 2, and the claims which depend from it, from the glycoproteins (and methods of using them) of the cited prior art.

As for the rejection over Hensel *et al.* (1999), *Cancer Res.* 59, 5299-5309 ("Hensel"), copies of the German priority documents for the instant application, DE19859248.5 and DE18909771.2, are attached, as well as verified translations thereof. The perfection of the claim for priority obviates the rejection over Hensel.

In view of the preceding arguments, it is believed that the application is in condition for allowance, which action is respectfully requested.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (twice amended) ~~A~~ An isolated glycoprotein that comprises at least one section of the amino acid primary structure of CD55 and a tumor-specific glycostructure.

5. (twice amended) ~~Use of a~~ A method for identifying a substance which binds to a glycoprotein according to claim ~~1 in a test process in which the ability of a substance to bind to the glycoprotein is determined~~ 2, comprising incubating a putative binding substance with said glycoprotein and determining if it binds specifically.

6. (amended) ~~Use~~ The method according to claim 5, further comprising determining ~~wherein~~ the ability of the tested substance to bind to the glycostructure of the glycoprotein ~~is determined~~.

7. (twice amended) ~~Use~~ The method according to claim 5 further comprising determining ~~wherein~~ the ability of the tested substance to induce apoptosis~~, especially in tumor cells, is determined~~.

9. (twice amended) ~~Use~~ The method according to claim 5, wherein the glycoprotein is ~~used~~ in an isolated form~~, as a cell extract, especially as a membrane preparation or in the form of complete cells, especially of human adenocarcinoma cell line 23132~~.

10. (twice amended) ~~Use~~ The method according to claim 5 for identifying a substance ~~substances~~ that binds ~~bind~~ specifically to a tumor ~~cells~~ cell.

11. (amended) ~~Use~~ The method according to claim 10 for identifying an agent ~~agents~~ for tumor diagnosis and/or tumor therapy.

12. (twice amended) ~~Use~~ The method according to claim 5, wherein the ~~pharmacologically compatible substances are tested~~ substance tested is pharmaceutically acceptable.

13. (amended) ~~Use~~ The method according to claim 12, wherein the tested ~~substances are selected from peptides~~ substance is a peptide, peptide mimetic ~~agents~~ agent, ~~antibodies~~ antibody, antibody ~~fragments and~~ fragment or antibody ~~derivatives~~ derivative.

14. (twice amended) ~~Use of substances that bind specifically to~~ A method for identifying an agent which induces apoptosis, comprising incubating a putative agent with a glycoprotein according to claim ~~1,~~ 2 ~~with the exception of~~ and determining if it binds specifically, wherein said putative agent is not the monoclonal antibody SC-1~~, for the production of agents that induce apoptosis~~.

15. (twice amended) ~~Use of substances that bind specifically to~~ A method for identifying an anti-tumor agent, comprising incubating a putative agent with a glycoprotein according to claim ~~1,~~ 2 ~~with the exception of~~ and determining if it binds specifically, wherein said putative agent is not the monoclonal antibody SC-1~~, for the production of anti-tumor agents~~.

16. (twice amended) ~~Use of substances that bind specifically to~~ A method for identifying an agent for tumor diagnosis, comprising incubating a putative agent with a glycoprotein according to claim ~~1,~~ 2 ~~with the exception of~~ and determining if it binds specifically, wherein said putative agent is not the monoclonal antibody SC-1~~, for the production of anti-tumor agents~~.

17. (twice amended) ~~Process~~ A method for preparation of ~~the agents~~ a pharmaceutical composition that induces ~~induce~~ apoptosis, ~~wherein a potentially active substance is tested on its ability for specific binding~~ comprising identifying an agent which binds specifically to a glycoprotein according to claim ~~1 and in the case of a positive test result, the substance is converted into a form for dispensing that is suitable for pharmaceutical applications optionally~~

~~together with common use adjucants, additives and vehicles~~ 2, and includes apoptosis, and combining it with a pharmaceutically acceptable adjuvant, additive and/or vehicle.

18. (twice amended) ~~Process~~ A process for the preparation of an anti-tumor ~~agents, wherein a potentially active substance is tested on its ability for specific binding~~ agent, comprising identifying an agent which binds specifically to a glycoprotein according to claim 2 ~~1~~ and combining it with a pharmaceutically acceptable adjuvant, additive or vehicle. ~~in the case of a positive test result, the substance is converted into a form for dispensing that is suitable for pharmaceutical applications optionally together with commonly used adjuvants, additives and vehicles.~~

19. (twice amended) ~~Process~~ A process for combatting tumors, comprising administering to a patient in need there of an anti-tumor-effective amount ~~action quantity~~ of a substance that ~~can bind~~ binds specifically to a glycoprotein according to claim 2 ~~1~~, with the exception of monoclonal antibody SC-1~~, is administered to a patient~~.

20. (twice amended) ~~Process~~ A process for the diagnosis of comprising contacting a sample or a patient tumor ~~tumors, wherein a sample that is to be tested or a patient who is to be tested is brought into contact~~ with a substance that ~~can bind~~ binds specifically to a glycoprotein according to claim ~~1~~ 2, and detecting , localizing and/or quantitating said ~~the presence, the localization and/or the quantity of the~~ glycoprotein in the sample or in the patient ~~is detected~~.

23. (twice amended) ~~Use of substances that specifically bind a glycoprotein according to claim 1~~ A method for inducing an apoptotic ~~processes~~ in a cell which does ~~that do~~ not comprise ~~any~~ cleavage of poly (ADP-ribose) - polymerase (PARP), comprising contacting said cell with a substance that specifically binds a glycoprotein according to claim 2.

24. (twice amended) ~~Use of substances~~ A method for inducing cell cycle arrest in a tumor cell, comprising contacting said tumor cell with a substance that specifically binds ~~bind~~ a glycoprotein according to claim 2 ~~1~~.

25. (twice amended) ~~Use of substances~~ A method for inducing apoptosis in a dormant tumor cell, comprising contacting said tumor cell with a substance that binds ~~bi nd~~ specifically to a glycoprotein according to claim 2 ~~1 for inducing apoptosis in dormant tumor cells~~.